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EXAMINER

VANDER VEGT, F

ART UNIT

PAPER NUMBER

1644

8

DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/322,352

Applicant(s)

Peschle et al

Examiner

F. Pierre VanderVegt

Group Art Unit

1644



☒ Responsive to communication(s) filed on Nov 6, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), ~~or thirty days, whichever is longer~~, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-70 ~~is~~/are pending in the application.

Of the above, claim(s) 12-17, 33-38, 45-50, 54-66, and 70 ~~is~~/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-5, 9, 18-27, 31, 32, 39-44, 51-53, and 67-69 ~~is~~/are rejected.

☒ Claim(s) 6-8, 10, 11, and 28-30 ~~is~~/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

This application claims priority to provisional application 60/087,153.

Claims 1-70 are currently pending in this application.

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Election/Restriction

1. Applicant's election without traverse of Group I, claims 1-11, 18-32, 39-44, 51-53 and 67-69, in Paper No. 7, filed November 6, 2000, is acknowledged.

Claims 12-17, 33-38, 45-50, 54-66 and 70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable
10 generic or linking claim. Election was made **without** traverse in Paper No. 7.

Claim Rejections - 35 USC § 112

wd. 2. Claims 9, 31, 32 and 44 are rejected under 35 U.S.C. 112, first paragraph, as containing
15 subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The monoclonal antibody (mAb) 260.4 recited in claims 9, 31 and 44 is essential to the claimed invention. The reproduction of mAbs from specific hybridomas is an extremely unpredictable event. The hybridoma producing the 260.4 mAb, disclosed on page 40 of the
20 specification, must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The instant specification does not disclose a repeatable process to obtain the mAb, and it is not apparent if the hybridoma is readily available to the public. If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such
25 assurances, or a statement by an attorney of record over his or her signature, stating that the hybridoma has been deposited under the Budapest Treaty and that the hybridoma will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the

record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample **or for the enforceable life of the patent**, whichever is longer. See 37 CFR 1.806. If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

Amendment of the specification to disclose the date of deposit and the complete name and address of the depository is required.

If the deposit was made after the effective filing date of the application for a patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed are the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from Applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the Applicant's possession at the time the application was filed.

Applicant's attention is directed to *In re Lundak*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985), and 37 CFR 1.801-1.809 for further information concerning deposit practice.

3. Claims 25 and 40-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Briefly, the claims are drawn to a method of identifying cells based upon the expression of [claim 25] or absence of [40-44] the "lin" marker. It is well recognized in the art that there is no singular cell-specific marker known by the acronym "lin," but the term is a generic one used for lineage specific markers. The acronym is used to designate a different set of markers based upon the subject matter of a particular report. Therefore, the term "lin" defines a potentially limitless

combination of cell-specific markers. While the instant specification discloses a group of cell-specific markers which Applicant regards as defining "lin" at, for example, pages 45-46, Applicant is reminded that, while claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore the claims read upon an infinite combination of markers defining cell lineages which the artisan could not know without undue experimentation given the paucity of guidance in the instant specification. Based upon the wide usage of the term "lin" in the art to define many different cell lineages, one of ordinary skill in the art at the time the invention was made would not be able to reasonably predict the scope of the cell types encompassed by the instant claims.

In view of the quantity of experimentation necessary, the nature of the invention, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute.

4. Claim 68 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claim is drawn to the isolation of KDR+ (VEGF RII+) cells based upon the co-expression of VEGF RI or VEGF RIII. The specification is not enabling for the claimed purification method. While it is recognized that the molecules are co-expressed on at least some cells, the extent of their co-expression is not clear from the instant specification. The antigens are not obligatory parts of a common complex. It is not readily apparent therefore that VEGFR II would be expressed on all the same cells as VEGF RI or VEGF RIII or vice versa. It would therefore constitute an undue burden on the part of one of ordinary skill in the art at the time the invention was made to determine whether the presence of VEGF RI or VEGF RIII on a cell type would be a reliable predictor for the presence of VEGF RII (KDR) on said cell.

5. Claims 2, 9, 25, 31, 32 and 39-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 2 is indefinite and unclear in the recitation of "pre-embryonic hematopoietic tissue."

5 The embryo stage begins with the fusion of an egg and a sperm to form a single cell. The egg and sperm are not hematopoietic in origin and are parentally derived. Therefore, there are no hematopoietic cells in the pre-embryonic stage. *all above cl 19*

W.D.
10 It is indefinite and ambiguous to recite the laboratory name "260.4" for the mAb in claims 9, 31 and 44, as laboratory names of monoclonal antibodies can be used by different artisans to designate different antibodies. It is suggested that the international depository accession number be recited in the claim. If desired, the international depository accession numbers may be followed in the claims by the laboratory names in parentheses. For example, the format --ATCC HB-XXXX (260.4)--, would be acceptable.

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15 Claims 25 and 40-44 are ambiguous and unclear in the recitation of the term "lin" [claim 25] or "lin" [40, 41]. The term lin is used in the art as a generic term to designate a lineage specific marker in regard to a particular direction of study. The meaning of the term is unclear, as different cell lines have different lineage specific markers which define their population. It is therefore unclear which cell lineage the claims are intended to exclude.

20 Claim 39 recites the limitation "select a population of CD34- cells" in line 3. There is no antecedent basis for this limitation in the claim. Base claim 24 recites "isolation of cells expressing an early marker using antibodies specific for said marker" and intervening claim 26 recites "wherein said early marker is CD34." Therefore, there is no antecedent basis for reciting the isolation of cells which are negative for the early marker CD34.

25 *Note*

6. Prior to setting forth any rejections over prior art references, it is noted here that the cell surface marker identified in the instant claims as "KDR" is also known in the art as "FLK-1," "VEGFR2," "VEGF RII," "FLK1/KDR" and "VEGFr-H."

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

5 A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the Applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10 8. Claims 1-3, 5, 18, 19, 22-24, 26, 27 and 67 are rejected under 35 U.S.C. 102(b) as being anticipated by Bhatia et al (14 on form PTO-1449).

The Bhatia et al reference teaches the isolation of a population of primitive human hematopoietic cells enriched for cells capable of repopulating in vivo. Bhatia teaches that the cells were selected on the basis of their being CD34+ and CD38-. While Bhatia does not specifically state that the cells express KDR, silence about a particular feature does not constitute absence of that feature. It is noted that the claims do not recite selection of the cells for the expression of KDR, rather KDR expression is recited as a property characteristic of the enriched cell population. Since KDR is a marker present on the surface of at least a subpopulation of CD34+ hematopoietic stem cells, enriching a population of hematopoietic stem cells for those which CD34+ necessarily enriches the population for KDR+ cells. The prior art teaching anticipates the claimed invention. *Maentan*

9. Claims 1-5, 18, 19, 21-27 and 67 are rejected under 35 U.S.C. 102(b) as being anticipated by Sutherland et al (63 on form PTO-1449).

25 The Sutherland et al reference teaches the isolation from bone marrow, cord blood or peripheral blood of a population of human hematopoietic stem cells enriched for cells capable of repopulating in vivo. Sutherland teaches that the cells were selected on the basis of their being CD34+ and negative for a variety of lineage specific markers (Abstract in particular). While Sutherland does not specifically state that the cells express KDR, silence about a particular feature *Maentan*

does not constitute absence of that feature. It is noted that the claims do not recite selection of the cells for the expression of KDR, rather KDR expression is recited as a property characteristic of the enriched cell population. Since KDR is a marker present on the surface of at least a subpopulation of CD34+ hematopoietic stem cells, enriching a population of hematopoietic stem cells for those which CD34+ necessarily enriches the population for KDR+ cells. The prior art teaching anticipates the claimed invention.

10. Claims 18, 26, 39 and 40 are rejected under 35 U.S.C. 102(a) as being anticipated by Zanjani et al (77 on form PTO-1449).

The Zanjani et al reference teaches the isolation of a CD34-Lin- population of cells (Figure 3 in particular) by isolating cells which did not stain with antibodies specific for CD34 or lineage specific markers. While Zanjani does not specifically state that the cells were KDR+, silence about a particular feature does not constitute absence of that feature and it is noted that the method of Zanjani is the same as that set out in claims 39 and 40 and therefore would result in the same end product. The prior art teaching anticipates the claimed invention.

11. Claims 1-5, 18, 22-27, 51-53 and 67 are rejected under 35 U.S.C. 102(b) as being anticipated by Brandt et al (17 on form PTO-1449).

The Brandt et al reference teaches the isolation from bone marrow of precursors human hematopoietic stem cells. Brandt teaches that the cells were selected on the basis of their being CD34+ and negative for a variety of lineage specific markers (Abstract in particular). Brandt further teaches the long-term culture of the cells and maintaining their hematopoietic potential by incubating in a medium comprising the growth factors IL-3, IL-3 and GM-CSF (Abstract in particular). While Brandt does not specifically state that the cells express KDR, silence about a particular feature does not constitute absence of that feature. It is noted that the claims do not recite selection of the cells for the expression of KDR, rather KDR expression is recited as a property characteristic of the enriched cell population. Since KDR is a marker present on the surface of at least a subpopulation of CD34+ hematopoietic stem cells,

enriching a population of hematopoietic stem cells for those which CD34+ necessarily enriches the population for KDR+ cells. The prior art teaching anticipates the claimed invention.

12. Claim 69 is rejected under 35 U.S.C. 102(b) as being anticipated by Matthews et al (46 on form PTO-1449).

The Matthews et al reference teaches the isolation of stem cells from fetal mouse liver. Matthews teaches the presence of Flk-1 (KDR) expression in highly purified stem cell populations from fetal liver which are both hematopoietic and non-hematopoietic in nature (paragraph bridging pages 9028-9029 and page 9030 in particular). Matthews further teaches that day 14 fetuses expressed Flk-1 in multiple non-hematopoietic cells from liver (oval cell) and cardiac (muscle) tissue. The prior art teaching anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 18, 26, 39 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Osawa et al (55 on form PTO-1449).

The Osawa et al reference teaches the isolation of a murine long-term repopulating CD34-Lin- population of cells (Figure 3 in particular) by isolating cells which did not stain with

antibodies specific for the murine equivalent of human CD34 or lineage specific markers. While Osawa does not specifically state that the cells were VEGFR2+, silence about a particular feature does not constitute absence of that feature and it is noted that the method of Osawa is the same as that set out in claims 39 and 40 and therefore would result in the same end product. While the teachings of Osawa were performed in mouse, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to isolate the same population of cells from a human subject as suggested by Osawa at page 244 in the statement "our findings have potential implications for the prospect of purification and expansion of human HSCs on the basis of CD34 expression as the sole criterion." One would have been motivated to perform such an isolation with a reasonable expectation of success based upon the fact that findings regarding hematopoietic stem cells in mice are applied to human stem cells.

14. Claims 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kabrun et al (39 on form PTO-1449).

The Kabrun et al reference teaches the isolation of Flk-1+ (KDR+) from murine embryonic yolk sac (Abstract in particular). Kabrun teaches that these cells represent an early population of hematopoietic stem cells. While the teachings of Kabrun were performed in mouse, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to isolate the same population of cells from a human subject. One would have been motivated to perform such an isolation with a reasonable expectation of success based upon the fact the Flk-1 expresses similarly on human and mouse hematopoietic stem cells that are isolated from cord blood or bone marrow. Therefore, the artisan would have predicted that the expression of KDR is also similar in embryonic yolk sack. Further, the findings regarding hematopoietic stem cells in mice are applied to human stem cells.

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Conclusion

15. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

16. Papers related to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for official documents to be entered into the record for Art Unit 1644 is (703)305-3014.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to F. Pierre VanderVegt, whose telephone number is (703)305-6997. The Examiner can normally be reached Tuesday through Friday and odd-numbered Mondays (on year 2000 366-day calendar) from 6:30 am to 4:00 pm ET. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ms. Christina Chan can be reached at (703)308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist, whose telephone number is (703)308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
Technology Center 1600
January 29, 2001



F. PIERRE VANDERVEGT
PATENT EXAMINER